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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FETTEROLF, BRANDON J	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 09/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/600,957	POWIS, GARTH	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) *1-6* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7 and 8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

The Election filed on July 24, 2006 in response to the Restriction Requirement of 6/23/2006 has been entered. Applicant's election of Group IV, claims 7-8, as specifically drawn to a composition comprising an agent that is useful in reducing or eliminating thioredoxin-associated apoptosis inhibition and an acceptable carrier has been acknowledged.

Applicants election of Group IV with traverse has been entered. The traversal is on the grounds that the search for each invention group will substantially overlap because each of the claims are directed to an inhibitor of thioredoxin expression. As such, Applicants assert that searching and considering the inventions as described in all the currently pending claims will not seriously burden the Examiner.

These arguments have been carefully considered, but are not found persuasive.

Regarding the question of burden of search, the Examiner recognizes, as noted in the Restriction Requirement, that the inventions are classified differently, which would necessitate different searches of the US Patents. Further, classification of subject matter is merely one indication of the burdensome nature of the search involved. For example, the literature search, particularly relevant in this art, is not coextensive and is much more important in evaluating the burden of search. Different searches and issues are involved in the examination of each group.

For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

Claims 1-8 are currently pending

Claims 1-6 have been withdrawn from consideration as being drawn to non-elected inventions.

Claims 7-8 are currently under consideration.

Note: During a telephone conversation with Ray Miller on 9/19/2006 a provisional election was made with traverse to prosecute the invention of small organic compounds recited in the specification on page 6 as required in the Restriction Requirement (page 2). Affirmation of this election must be made by applicant in replying to this Office action. For prior art purposes, claims 7-8 will be examined to the extent that they are drawn to small organic compounds.

Information Disclosure Statement

The Information Disclosure Statement filed on 1/07/2004 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. A signed copy of the IDS is attached hereto.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are inclusive of a genus of agents that reduce or eliminate thioredoxin-associated apoptosis. Therefore, the claims encompass a genus of molecules defined solely by its principal biological property, which is simply a wish to know the identity of any material with that biological property. However, the written description in this case only reasonably conveys antibodies against thioredoxin and/or thioredoxin reductase, anti-sense thioredoxin and/or anti-sense thioredoxin reductase compounds and compounds that inhibit the activity of this thioredoxin, wherein the compound that inhibits the activity of thioredoxin are 2-imidazolyl disulfides.

The Written Description Guidelines for examination of patent applications indicates, "the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical characteristics and/or other chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus." (Federal register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3) and (see MPEP 2164).

The specification teaches (page 6, last paragraph) that compounds that inhibit thioredoxin include, but are not limited to, antibodies to thioredoxin and compounds that inhibit the activity of thioredoxin. The specification further teaches (page 8, 5th and 6th paragraphs) that antibodies, as well as anti-sense compounds, against thioredoxin or thioredoxin reductase are useful as anti-tumor agents. In addition, the specification teaches unsymmetrical 2-imidazoyl disulfides inhibit thioredoxin (page 36, 4.4.1). Thus, while the specification reasonably conveys antibodies and antisense compounds against thioredoxin or thioredoxin reductase, as well as unsymmetrical 2-imidazoyl disulfides as agents useful for reducing or eliminating thioredoxin-associated apoptosis inhibition, the specification does not appear to be commensurate in scope with the instantly claimed genus. Accordingly, there is insufficient written description encompassing an "agent useful in reducing or eliminating thioredoxin-associated apoptosis inhibition" because the relevant identifying characteristics of the genus such as structure or other physical and/or chemical characteristics of an "agent useful in reducing or eliminating thioredoxin-associated apoptosis inhibition" are not set forth in the specification as-filed. A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or by describing structural features common the genus that "constitute a substantial portion of the genus." See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997): "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cNDA, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The court has since clarified that this standard applies to compounds other than cDNAs. See University of Rochester v. G.D. Searle & Co., Inc., __F.3d__,2004 WL 260813, at *9 (Fed.Cir.Feb.

13, 2004). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features that are common to the genus. That is, the specification provides neither a representative number of agents that encompass the genus of agent useful in reducing or eliminating thioredoxin-associated apoptosis inhibition nor does it provide a description of structural features that are common to the agents. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure is insufficient to describe the genus. Thus, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure(s) of the encompassed genus of agent useful in reducing or eliminating thioredoxin-associated apoptosis inhibition, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only antibodies against thioredoxin and/or thioredoxin reductase, anti-sense thioredoxin and/or anti-sense thioredoxin reductase compounds and compounds that inhibit the activity of this thioredoxin, wherein the compound that inhibits the activity of thioredoxin are 2-imidazolyl disulfides, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 7-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Oblong et al. (Cancer Chemotherapy and Pharmacology 1994; 34: 434-438, *IDS*).

Oblong et al. teach a composition comprising an agent and an acceptable carrier, wherein the agent acts as a reversible inhibitor of human thioredoxin (page 436, 1st column, 1st full paragraph and Title). With regards to the thioredoxin inhibitor, the reference teaches that the thioredoxin inhibitors are alkyl 2-imidazole disulfide analogues (Title and page 435, Fig. 1). Moreover, the reference teaches that the alkyl 2-imidazolyl disulfide analogues are useful at inhibiting cellular proliferation, e.g. cell growth (page 437, Fig. 4A,B and 2nd column, last paragraph). Thus, while Oblong et al. do not explicitly teach that the agent is useful in reducing or eliminating thioredoxin-associated apoptosis inhibition, the intended use of the compound must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. A composition is a composition irrespective of what its intended use is. See In re Tuominen, 213 USPQ 89 (CCPA 1982).

Claims 7-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Mau et al. Biochemical Pharmacology 1992; 43 (7): 1613-1620, *IDS*).

Mau et al. teach a composition comprising an agent and an acceptable carrier, wherein the agent acts as a reversible inhibition of rat liver thioredoxin reductase (Title and page 1614, 1st column, *Assays*). With regards to the agents, the reference teaches that the agents include, but are not limited to, quinoids such as diaziquone, doxorubicin, 2,6-dichloroindophenol and streptonigrin (page 1614, 2nd column, *Inhibition of TR by quinoids*). Thus, while Mau et al. do not explicitly teach that the agent is useful in reducing or eliminating thioredoxin-associated apoptosis inhibition or

inhibiting thioredoxin stimulated cell growth, the intended use of the compound must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. A composition is a composition irrespective of what its intended use is. See In re Tuominen, 213 USPQ 89 (CCPA 1982).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 7-8 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 4, 5 and 7 of copending Application No. 10/617,949.

Although the conflicting claims are not identical, they are not patentably distinct from each other because a species anticipates a genus. The species composition comprising an asymmetric disulfide or derivative thereof, wherein said asymmetric disulfide is an inhibition of thioredoxin or thioredoxin reductase claimed in the conflicting patent application appears to fall within the same scope of the genus composition comprising an agent that is useful in reducing or eliminating thioredoxin associated apoptosis inhibition claimed in the application being examined.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Therefore, NO claim is allowed.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Kirkpatrick et al. (Eur. J. Med. Chem. 1992; 27: 33-37) teach the synthesis and evaluation of imidazolyl disulfides for selective cytotoxicity to hypoxic EMT6 tumor cells in vitro. Specifically, the reference teaches a composition comprising imidazolyl disulfides dissolved in DMSA (page 37, 1st column, *Biological methods*).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brandon J Fetterolf, PhD
Patent Examiner
Art Unit 1642

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER

BF
September 20, 2006